

IT IS CLAIMED:

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1. A method of identifying genetically modified mammalian cells comprising the steps of:
a) introducing a nucleic acid sequence encoding a mutated protein-tyrosine kinase receptor (PTKR) operatively linked to an expression control sequence into a cell to form a genetically modified cell, wherein the mutated PTKR either comprises a modification to the intracellular and the extracellular domains, or excludes any nerve growth factor receptor(s) (NGFR) and comprises a modification to the intracellular domain;
b) allowing expression of the mutated PTKR in the genetically modified cell; and
c) identifying said genetically modified cell expressing the mutated PTKR.

2. The method according to claim 1, wherein the mutated PTKR is selected from a mutated epidermal growth factor receptor (EGFR) family member and muscle specific tyrosine kinase receptor (MuSK-R) family member.

3. The method according to claim 2, wherein the mutated EGFR family member is a mutated EGFR1, optionally selected from the sequence designated EGFR1-I and EGFR1-II.

20 4. The method according to claim 2, wherein the mutated MuSK-R is selected from the sequence designated mMmSK-RI and mMmSK-RII.

5. The method according to any preceding claims, wherein the mutated PTKR is truncated from the intracellular domain, and optionally also from the extracellular domain.

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6. The method according to claim 2, wherein the introducing step is accomplished by incorporating the nucleic acid sequence encoding the mutated EGFR or MuSK-R into a vector and introducing said vector into said cell.

7. The method according to claim 6, wherein the vector is a retroviral vector.

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8. The method according to claim 1, wherein said identifying step is accomplished by contacting the genetically modified cells with an antibody that recognizes and binds to the mutated PTKR.

9. The method according to claim 1, wherein the identifying step separates the genetically modified cells from the non-genetically modified cells.

10. The method according to claim 1, further comprising the step of separating the identified cells expressing the mutated PTKR.

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11. The method according to claim 1, wherein the cells are human cells.

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12. The method according to claim 11, wherein the cells are selected from the group consisting of hematopoietic cells, liver cells, endothelial cells and smooth muscle cells.

13. The method according to claim 11, wherein the cells are hematopoietic cells.

14. The method according to claim 13, wherein the cells are hematopoietic cells are stem cells or T-cells.

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15. The method according to claim 6, wherein a heterologous gene is also incorporated into said vector.

16. A method of identifying genetically modified mammalian cells comprising the steps of:

- incorporating into a vector a nucleic acid sequence encoding a mutated protein-tyrosine kinase receptor (PTKR) family member, wherein said PTKR either comprises a modification to the intracellular and the extracellular domains, or excludes any nerve growth factor receptor(s) (NGFR) and comprises a modification to the intracellular domain; introducing the vector into a mammalian cell to form a genetically modified cell;
- allowing expression of the mutated PTKR in the genetically modified cell; and

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c) identifying said genetically modified cell expressing the mutated PTKR.

17. The method according to claim 16, wherein the mutated PTKR is selected from EGFR, preferably EGFR1-I or EGFR1-II, and MuSK-R, preferably mMmSK-RI or mMmSK-RII.

18. The method according to claim 16, wherein the vector is a retroviral vector.

19. The method according to claim 16, wherein a heterologous gene is also incorporated into said vector.

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20. A method for the immunoselection of transduced mammalian cells comprising,

- a) retrovirally transducing mammalian cells with a nucleic acid sequence encoding a protein-tyrosine kinase receptor (PTKR) family member operatively linked to an expression control sequence; wherein said PTKR either comprises a modification to the intracellular and the extracellular domains, or excludes any nerve growth factor receptor(s) (NGFR) and comprises a modification to the intracellular domain;
- b) incubating the transduced cells with a marked antibody which recognizes and binds specifically to the mutated PTKR; and
- c) identifying the marked transduced cells.

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21. The method according to claim 20, wherein the cells are human cells or hematopoietic cells.

22. The method according to claim 20, wherein the mutated PTKR is selected from EGFR, preferably EGFR1-I or EGFR1-II, and MuSK-R, preferably mMmSK-RI or mMmSK-RII.

23. The method according to claim 20, wherein the cells are transduced by a retroviral vector derived from the group consisting of moloney murine leukemia virus (MoMLV), myeloproliferative sarcoma virus (MPSV), murine embryonic stem cell virus (MESV), murine stem cell virus (MSCV) and spleen focus forming virus (SFFV).

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24. The method according to claim 20, wherein the cells are transduced by a vector derived from a lentivirus.
25. The method according to claim 20, further comprising the step of separating the identified marked transduced cells from non-marked cells.
26. The method according to claim 20, further comprising the step of expanding the marked transduced cells.
- 10 27. A method of identifying mammalian cells expressing a protein of interest, comprising the steps of,
- introducing into a mammalian cell a nucleic acid encoding a nucleic acid comprising a DNA sequence encoding a protein of interest and encoding a protein-tyrosine kinase receptor (PTKR) family member operatively linked to an expression control sequence, wherein said PTKR either comprises a modification to the intracellular and the extracellular domains, or excludes any nerve growth factor receptor(s) (NGFR) and comprises a modification to the intracellular domain;
 - culturing the resulting mammalian cells; and
 - identifying cells which express the mutated PTKR thereby obtaining cells which express the protein of interest.
- 20 28. The method according to claim 27, wherein the mutated PTKR is selected from EGFR, preferably EGFR1-I or EGFR1-II, and MuSK-R, preferably mMmSK-RI or mMmSK-RII.
29. The method according to claim 27, wherein the nucleic acid encoding the mutated PTKR and the nucleic acid encoding the protein of interest in step (a) are introduced on a retroviral vector.
30. A mutated muscle specific tyrosine kinase/receptor (MuSK-R) family member which is truncated within the cytoplamic domain, preferably mMmSK-RI or mMmSK-RII.

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